

REMARKS/ARGUMENTS

The Status of the Claims.

Claims 31, 34, 35, 39, 41 to 44, 46 to 49, 51 and 54 to 61 are pending with entry of this amendment. Claims 1 to 30, 32, 33, 36 to 38, 40, 45, 50, 52 and 53 are cancelled. Claims 59 to 61 being added herein. Claims 31, 35, 43, 46, 47, 51, 56 and 57 are amended herein. These amendments introduce no new matter and support is replete throughout the specification. These amendments are made without prejudice and are not to be construed as abandonment of the previously claimed subject matter or agreement with any objection or rejection of record.

With respect to claim 31 and 47, the deletion of the 4-nitro amino acid tailors the listed unnatural amino acids to those configured to compliment the O-RS of the claim structured to function with meta-substituted amino acids. The O-RS structured to compliment the meta-substituted amino acids can be found throughout the specification. For example, see specification at paragraphs 14, 26, and 52; Example 1 starting at paragraph 185; and Figure 6.

Claim 35 is merely adjusted to reflect the deletion of the 4-nitro amino acid from the parent claim.

The two or more redox amino acid aspect has been moved from the parent claim to new claim 61. Claim 43 is amended to reflect this change in parent claim 31.

Claim 51 is amended to correct dependency in light of the claim 50 cancellation.

Support for the 90% identity aspect of amended claim 56 can be found, e.g., at paragraphs 14 and 122.

Claims 57 and 58 are amended to provide proper antecedent reference.

Support for new claim 59 can be found, e.g., throughout the specification and in Example 1.

Support for new claim 60 can be found throughout the specification, in Example 1 and in the Figures.

Applicants submit that no new matter has been added to the application by way of the above Amendment. Accordingly, entry of the Amendment is respectfully requested.

Interview Summary.

Applicant's Representative, Gary Baker, briefly discussed the present case with Examiner Gebreyesus on June 10, 2009 by telephone. Claim 31 was discussed. Applicant's Representative outlined proposed claim 31 aspects, as presented in the amendment herein. The Examiner generally suggested that enablement is more likely where structures of limited percent identity specifically function in combination with components of complementary structure.

35 U.S.C. §103(a).

Claims 31, 34, 35, 39, 41 to 44, 46 to 48 and 50 to 58 were rejected under 35 U.S.C. §103(a) as allegedly obvious based on Schultz (U.S. 7,045,337) in light of Rodriguez (Biochem. J., 149: 115-121; 1975). To the extent the rejection is deemed applicable to the amended claims, Applicants traverse.

A proper analysis under the recently reaffirmed *Graham v John Deere* standard demonstrates the non-obviousness of the invention. According to the Supreme Court in *KSR International Co v. Teleflex* (550 U.S. 398 (2007); 127 S. Ct. 1727, 1740-41, 82 USPQ2d 1385-1396 (US 2007)), the appropriate standard for analyzing questions of obviousness is that:

the scope and content of the prior art are determined, differences between the prior art and the claims at issue are analyzed and the level of ordinary skill in the pertinent art is resolved. Against this background the obviousness or non-obviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unresolved needs, failure of others, etc. might be utilized to give light to the circumstances surrounding the origin of the subject matter to be patented.

Id. quoting *Graham v. John Deere of Kansas City* 383 U.S. 1, 17-18.

The current Examination Guidelines (e.g., MPEP 2143) and *KSR* require the Office in an obviousness rejection to provide a statement as to why one of skill would have

combined known elements. Further, an obviousness rejection must include fact-based findings demonstrating: 1) a combination of reference elements describing each limitation of the claims, 2) known elements that function in the same way in the combination as in the references themselves, 3) the elements are combined by known methods, 4) the result of the suggested combination of elements would have been predictable, and 5) one of skill in the art would have expected success in providing the claim in light of the references. Here, the rejection fails each of these requirements, as applied to the *Graham* factors.

Schultz is alleged to teach incorporating various unnatural amino acids into proteins of interest; incorporation of one or more unnatural amino acids; and redox unnatural amino acids. The Office notes that "Schultz et al do not specifically teach a protein composition comprising at least two or more different redox active amino acids including those" of the claims.

Rodriguez binds a single DHP to the C-terminus of some proteins in a brain homogenate according to a mode of action not understood. Rodriguez is offered to "show that the redox active unnatural amino acid ...(DHP) can be incorporated into a protein in such a way as to exclude the incorporation of L-tyrosine." The allegations of the Office do not cure the defects of Schultz with regard to the previous claims, much less the currently amended claims.

As a preliminary Matter, Applicants note that although claim 49 is nominally rejected in the Office Action Summary sheet, it is not actually rejected in the Action itself.

Not all limitations of the amended claims have been alleged. Although it has been alleged that RSs may be provided with 90% identity to SEQ ID NO: 1, there is no allegation on the record regarding the limitations directed to the aspects of particular mutations at particular positions of the sequence. For example, there is no allegation of at least one orthogonal aminoacyl-tRNA synthetase (O-RS) comprising a Leu amino acid in a position of the O-RS corresponding to Tyr32 of SEQ ID NO: 4, a Ser amino acid residue in a position of the O-RS corresponding to Ala67 of SEQ ID NO: 4, an Asn amino acid residue in a position of the O-RS corresponding to His70 of SEQ ID NO: 4, or a Gln residue in a position of the O-RS corresponding to Ala167 of SEQ ID NO: 4.

The Action has not alleged a motivation for one of skill in the art to attempt the combination suggested in the rejection. For example, just because DHP existed before the present invention and was inexplicably incorporated singly to the C-terminus of a protein, this would not have motivated one of skill to provide unnatural redox amino acid incorporation by translation, and would not motivate one to somehow provide the specific mutant components of the currently amended claims. Further, Rodriguez merely observed the unexplained phenomenon of C-terminus incorporation without any suggestion of a motivating utility for the product.

Regarding combination with Rodriguez, the cited DHP functions differently in the reference than in the suggested combination, therefore the combination is not obvious according to *KSR*. For example, where Rodriguez is cited by the Office as providing a component to function in Schultz, it is well settled law that the component must be taught as possessing that function required by the logic of the allegation. According to *In re Keller* (citing *In re Young*, 159 USPQ 725 (CCPA 1965)), an aspect of a secondary reference combined to allege obviousness with a primary reference must include those known properties required to complete the allegedly obvious combination. That is, it is not "attacking the references individually" where an Applicant argues aspects of a secondary reference component that are aspects necessary to cure the defect in the primary reference. Here, Rodriguez does not support obviousness because it does not teach redox amino acids functioning as substrates for incorporation, as required in the Office rationale to compliment the primary reference. In Rodriguez is not clear how the redox amino acid functions in the C-terminus incorporation described. However, it is clear that the unnatural redox amino acid is not taught as functioning as a substrate for the particular O-RS of the claims. Moreover, with regard to certain dependent claims, the redox amino acid is taught not to function for incorporation at two or more positions in a peptide or at a position other than a C-terminus.

Because the present claims include specific mutations in functional combination with other components, it would be unreasonable to suggest a generic teaching of screening would obviously provide the particular claimed composition. For example, the outcome of various screening procedures would not necessarily be the same, so the same result is not inherent, or even likely, in the cited teachings. One of skill in the art would

predict that the outcome of a particular screening would not result in the exactly same combination mutations, e.g., as found in the claims. Therefore, the claimed compositions are not predictable, and there would not be an expectation of success in providing the same RSs of the claims.

Double Patenting.

Claims 31, 46, 48, and 50 to 58 have been rejected based on the judicially created doctrine of obviousness-type double patenting in light of Schultz '337. To the extent the currently amended claims are deemed obvious, Applicants traverse.

Applicants note that the present claims can not be considered to involve obviousness type double patenting for the reasons discussed above.

CONCLUSION

In view of the foregoing, Applicants believes all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the claims are deemed not to be in condition for allowance after consideration of this Response, a telephone interview with the Examiner is hereby requested. Please telephone the undersigned at (510) 769-3510 to schedule an interview.

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Respectfully submitted,



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Attachments:

- 1) A transmittal sheet; and,
- 2) A receipt indication postcard.